REMARKS

Applicants are in receipt of the Office Action mailed March 12, 2007, and have the following comments.

Rejection pursuant to 35 USC §102(b)

The Examiner has not repeated the rejection of claims 31-36, 39-46 and 49-50 as allegedly anticipated over Loftsson et al., U.S. Patent. No. 5472,954. Applicants thank the Examiner for having withdrawn this ground of rejection.

Rejection pursuant to 35 USC §103(a)

The Examiner has rejected claims 31-50 as allegedly obvious over Loftsson further in light of Dziabo et al., U.S. Patent No. 5,424,078. The Examiner alleges that Loftsson et al. teaches a preserved cyclodextrin and prednisolone ophthalmic composition, and that Dziabo et al. disclose chlorite as a preservative. The Examiner contends that a) Loftsson discloses a preserved cyclodextrin and prednisolone composition and it would have been obvious to one of ordinary skill in the art to employ the chlorine dioxide disclosed in Dziabo as a preservative in an ophthalmic preparation.

The Examiner states that Loftsson does not teach predinsolone acentate, the active agent of the present claims. However, the Examiner indicates that Loftsson teaches a "small genus, prednisolone, thus the speciels claimed, prednisolone acentate, would have been immediately envisioned. Applicants respectfully tranverse this rejection for the following reasons.

As an initial matter, Applicants hereby incorporate by reference the arguments made in the Reply filed August 21, 2006 in this case. In these arguments, Applicants have maintained that prednisolone acentate is not a species of the genus "prednisolone", but is rather a different and distinct chemical compound from prednisolone.

Applicants hereby submit the attached Declaration of Ken Chow, Ph.D., one of the inventors of the present invention, in which Dr. Chow indicates that one of ordinary skill in the art of medicinal chemistry would certainly have understood at the priority date of the present application that the compounds prednisolone and prednisolone acetate are separate and distinct chemical entities.

As discussed above, the Loftsson reference does not disclose an ophthalmic composition containing the compound being claimed in the present claims, prednisolone acetate. This fact is supported by the 13th edition of the Merck Index, page ix and Monograph 7807, which have been made of record herein.

The Manual of Patent Examining Procedure (MPEP), relying on long-established judicial precedent, states that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so in the references or otherwise within the knowledge of the person of ordinary skill in the art. See MPEP § 2143.01. As indicated more fully below, there is nothing in Loftsson et al., or in the combination of Loftsson and Dziabo et al., that would suggest the specifically claimed compositions containing prednisolone acetate, a compound not even mentioned in either reference, or methods of using such compositions. For this reason, the Applicants respectfully request the Examiner to withdraw this rejection and permit the present claims to proceed to issue.

Applicants have submitted with this Reply a Supplemental Information Disclosure Statement placing two references into the record. These references are Loftssona et al., Advanced Drug Delivery Review 36 (1999) 59-79 and Lyons et al., U.S. Patent Publication No. 2005/0234018.

Both of these references provide evidence that the claimed prednisolone acetate-containing compositions of the present invention yield surprising results when used as a ophthalmic composition.

Loftssona et al. discusses the use of cyclodextrins with an active drug for ophthalmic drug delivery. While the publication discusses that cyclodextrins may be useful additives in ophthalmic

formulations, some disadvantages of cyclodextrin use in ophthalmic formulations are clearly disclosed in this publication. For example, *Loftssona et al.* discusses that "[i]t is generally accepted that only the free drug, and not the drug/CD complex, can penetrate lipophilic biological barriers", such as the cornea. *Loftssona et al.* at 70, second column at 8.1. Moreover, this reference discloses "corticosteroids can only be administered locally for diseases of the outer eye and anterior segments of the eye. For diseases of the posterior segments of the eye, systemic administration is required." *Id.* at 74.

However Lyons et al., filed and published after the priority date of the present invention, proves otherwise. In Figure 2 of Lyons et al. one 35 µl drop of one of seven cyclodextrin-prednisolone acetate preparations are instilled into rabbit eyes and after 60 minutes the amount of prednisolone acetate and its metabolites prednisolone and prednisone in rabbit aqueous humor is determined and the sum reported for each preparation. Figure 3 shows the results of assaying the vitreous humor of the same animals at the same time point – this time the amount of the metabolite prednisolone is determined. As can be seen, in the absence of cyclodextrin prednisolone acetate is unable to enter the vitreous (posterior) chamber (Figure 3, bar 2g). However, the compositions containing even half as much prednisolone acetate in combination with cyclodextrin show substantial infusion into the posterior segment (Figure 3, bar 2b).

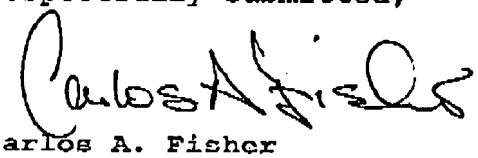
Thus, contrary to the prevailing opinion of the prior art, the combination of cyclodextrin with prednisolone acetate facilitates

delivery of the drug to the vitreous humor and the posterior segment of the eye. These results are completely unanticipated, surprising and non-obvious.

CONCLUSION

For the above reasons Applicants submit that the claims hare in condition for allowance and respectfully request that the Examiner issue a notice to that effect. Applicants also request a one-month extension of time to reply to the March 12, 2007 Office Action, and hereby authorize the Commissioner to use Deposit Account 01-0885 for the payment of this or any other fee now due in connection with this communication.

Respectfully submitted,



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